

Formulation and Dosage Form Providing Increased Bioavailability of Hydrophobic Drugs Liang C. Dong, Ruiping Zhao, and Patrick S. L. Wong U.S. Application No. 10/698,894

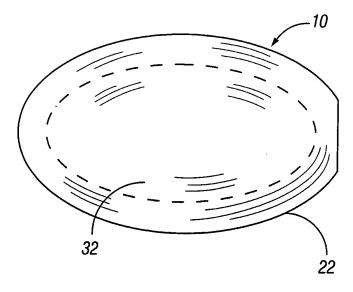


FIG.1

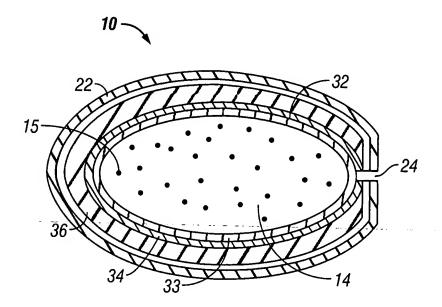


FIG.2

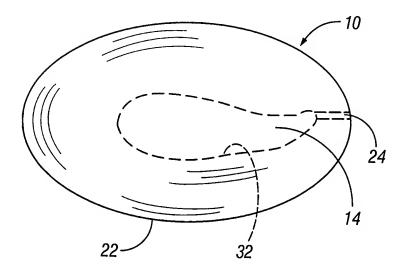


FIG. 3

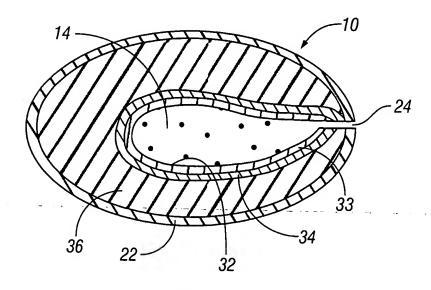
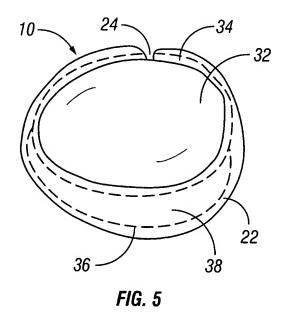


FIG. 4



33 34 33 34 36 38 22

FIG. 6

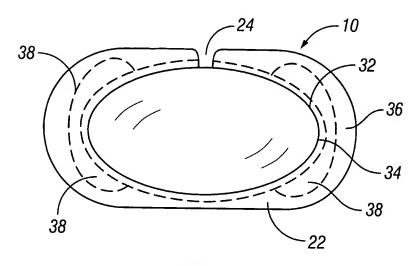


FIG. 7

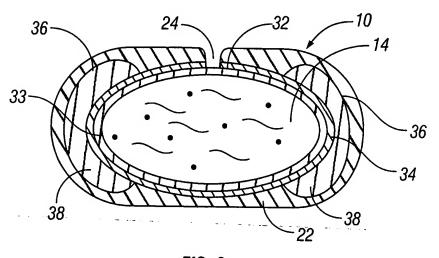
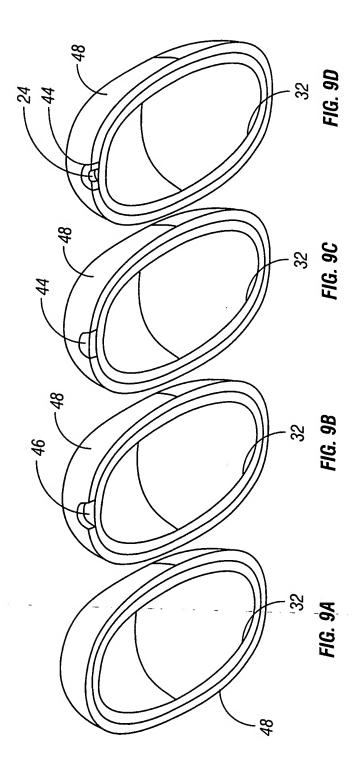


FIG. 8

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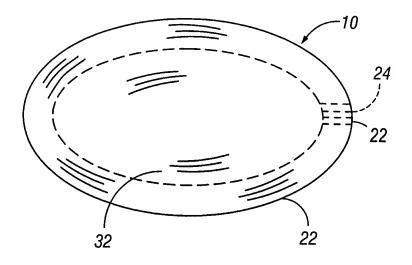


FIG. 10

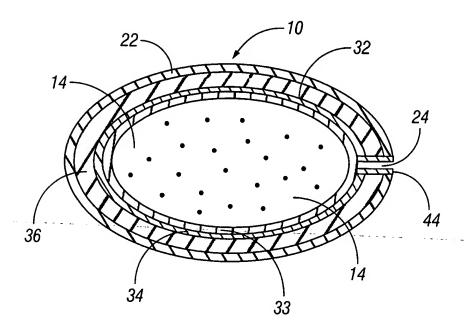


FIG. 11

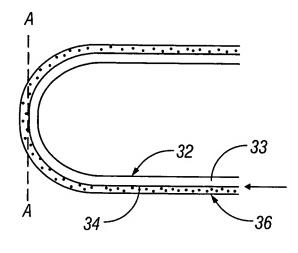


FIG. 12

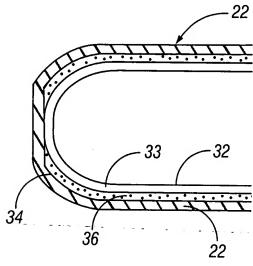


FIG. 13

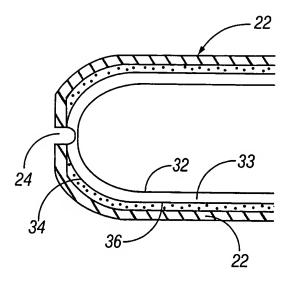


FIG. 14

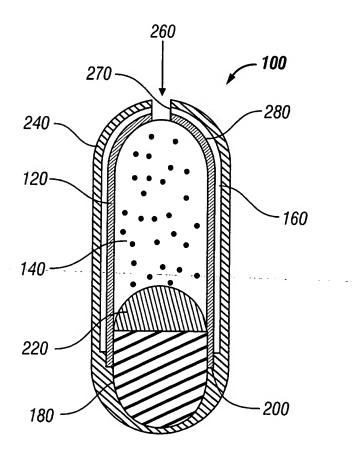


FIG. 15

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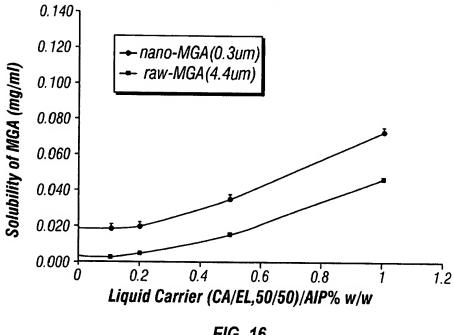
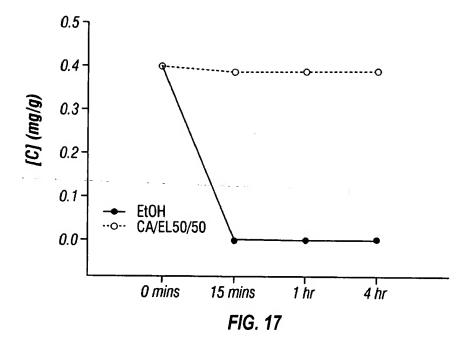
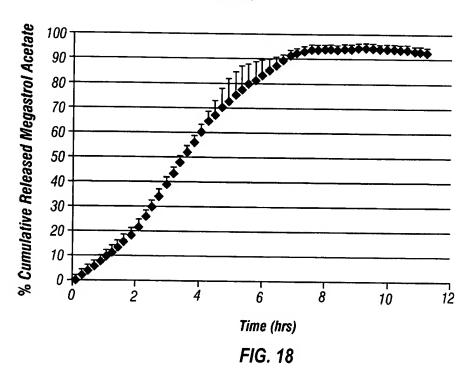
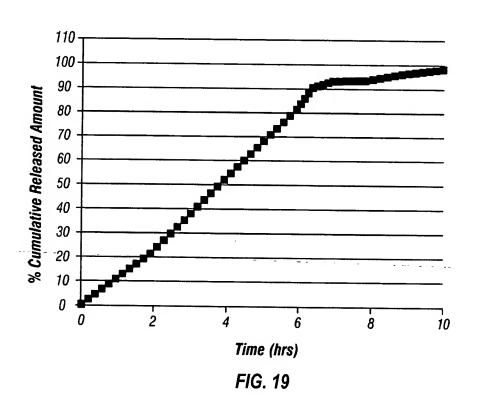


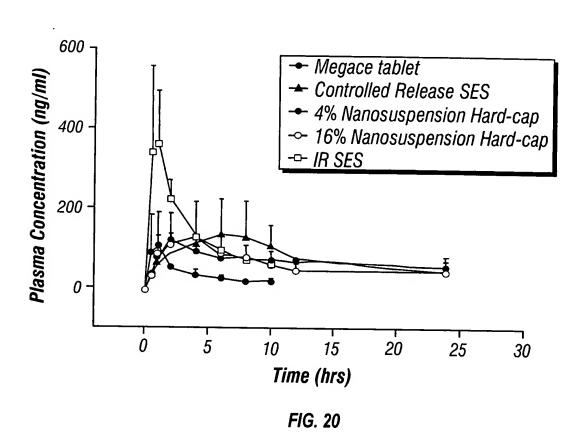
FIG. 16











Physical Properties of Various Saturated Fatty Acids

Fatty Acid	Melting temperature (°C)	Solubility in water at 20°C (mg/g)
Caproic acid (C6)	-3.4	10.82
Caprylic acid (C8)	16.7	0.68
Capric acid (C10)	31.4	0.15
Lauric acid (C12)	44	Insoluble
Myristic acid (C14)	58.5	
Palmitic acid (C16)	63-64	Insoluble
Stearic acid (C18)	69-70	Very slightly soluble

FIG. 21

Composition of Dosage Megastrol Acetate Formulations of Dosage Forms Used in Multi-arm PK Study

	Formulation
Megace Tablet (20mg)	Unknown
IR SES (10mg) x2	MA/Pluronic F108/Capric Acid/Cremophor EL
	(1.77/0.83/48.7/487, wt%)
Controlled Release SES (10mg) x2	MA/Pluronic F108/Capric Acid/Cremophor EL
	(1.77/0.83/48.7/48.7, wt%)
4% Nanosuspension Hard-cap	MA/Pluronic F108/Capric Acid/Cremophor EL
(20 mg)	(3.8/1.4/47.4/47.4, wt%)
16% Nanosuspension Hard-cap	MA/Pluronic F108/Capric Acid/Cremophor EL
(20 mg)	(16.0/4.2/39.9/39.9, wt%)

Plasma Sample Analysis (LC-MS) Conditions

HPLC Conditions	HPLC: Agilent 1100 (ID: LC-125) Column: MetaChem Polaris C18-A, 100x30mm, 3um. Guard Column: Metaguard Polaris C18-A,4.6mm, 3um. Flow Rate: 0.35ml/min. Injection Volume: 40ul. Mobile Phase: Isocratic 60/40 CH3CN/H2O, 0.2% Formic Acid.
MS Conditions	MS: PE Sciex API 300 LC/MA/MA with Analyst Ion Source: TurbolonSpray Scan Type: Positive MRM. Curtain Gas: Nitrogen, 9. Nebulizer Gas: Nitrogen, 9. Ionspray Voltage: 5.0 kV. Declustering Potential: 22V. Collision Gas: Nitrogen, 2. Collision Energy: 15V. MRM: m/z 385.2 to 325.2 for MA, 400ms. M/z 315.1 to m/z 109.0 for internal standard, 400ms.